UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,535	09/01/2006	Piet Herdewijn	50304/138001	6995

21559 7590 12/03/2009

CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
CRANE, LAWRENCE E	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
12/03/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/598,535	HERDEWIJN ET AL.	
	Examiner	Art Unit	
	Lawrence E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *September 1, 2006(preliminary amendment)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 September 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/26/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The Abstract of the Disclosure is objected to because is does not meet the requirement of the MPEP for US application. Correction is required. See MPEP §608.01(b).

Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts, compounds or compositions, the general nature of the compound or composition should be given as well as its use, e.g., "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary. Complete revision of the content of the abstract is required on a separate sheet.

Applicant is respectfully requested to amend the abstract because this document is presently not in US format. In addition, the abstract is to brief, not mentioning all of the various parts of the instant claimed subject matter.

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed. In addition, the "Brief Descriptions of the Drawings is far too brief. Examiner respectfully suggests that each drawing needs a separate description, and that each separate description should include process information for steps provided for but not described in the figure. Alternatively, applicant may elect to add process conditions for steps not specifically described on the face of the figure by adding these details to an amended version of the actual figure.

The instant disclosure fails to include "Cross-References to Related Applications." See 37 C.F.R. §1.78 and MPEP at §201.11. Applicant is respectfully requested to include the requested information as the first paragraph of the disclosure.

Claims **1-13** have been cancelled, no claims have been amended, the disclosure has not been amended at page 1, and new claims **14-26** have been added as per the preliminary amendments filed September 1, 2006. One Information Disclosure Statement (1 IDS) filed September 26, 2006 has been received with all cited non-US patent references and made of record.

Claims **14-26** remain in the case.

Note to applicant: when a rejection refers to a claim **X** at line y, the line number "y" is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

35 U.S.C. §101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title."

Claims **22 and 23** are rejected under 35 U.S.C. §101 because the noted method claims lack a demonstrated utility or operable utility because of the presence of the term "prevention" when the instant disclosure fails to adequately establish that the instant claimed methods of treatment are capable of preventing any viral infection, or to prevent an HIV infection specifically.

In addition, claims **20 and 26** the definitions of the variable "V" as "silyl" must be read to include structural alternatives wherein Si-H bonds are present, thereby rendering the compounds being claimed pyrophoric (spontaneously flammable in air). As a consequence a substantial portion of the compounds being claimed appear to lack reasonable utility for the purpose intended in view of their excessive oxygen sensitivity.

Claims **22, 23 and 25** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Factors to be considered:

a) Actual Reduction to Practice? The instant disclosure includes a single pair of compounds tested for anti-HIV activity at page 97, does not include any tests of any other viruses, and does not include any tests establishing that any of the instant compounds is capable of preventing any viral infection. In addition, there are no tests of any compound newly disclosed herein in combination with any other antiviral agent (claim **25**) or a showing that any such a combination has a utility in the treatment of any disease condition.

b) Disclosure of Drawings or Structural Chemical Formulas? This topic is not relevant to the present analysis of the instant claimed subject matter.

c) Sufficient relevant identifying characteristics? This topic is not relevant to the present analysis of the instant claimed subject matter.

d) Method of making the claimed invention? This topic is not relevant to the present analysis of the instant claimed subject matter.

e) Level of skill in the art? This topic is not relevant to the present analysis of the instant claimed subject matter.

f) Predictability in the art? The minimal amount of data provided by applicant and the minimal amount of data in the prior art relevant to the instant claims support the view that the instant art area is presently highly unpredictable.

For the above reasons, the instant cited claims have been found to be lacking in proper support from the instant written description.

Claims **14-20 and 22-26** are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for the synthesis of a small number of nucleoside and nucleotide analogues wherein linker-attached 3-phosphonyl-L-threofuranosyl moieties have replaced ribo- or 2'-deoxyribofuranosyl substituents, for the synthesis thereof, for the pharmaceutical compositions thereof, and for the treatment of HIV therewith, does not reasonably provide enablement for the synthesis, or the effective anti-viral administration of, nearly all of the vast array of compounds claimed herein, wherein the scope of the claimed subject matter is further complicated by the presence of indefinite terms including "derivatives," and several substituent definitions that fail to completely define the substituents in question because of the presence of functional terminology: e.g. the term "Phos" in claim **20**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8

USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims is found to be excessive because the definitions of structural variables, and the definition of diseases claimed to be effectively treated, are much more comprehensive and broad in scope that the small number of specific embodiments provided herein.

B. The nature of the invention: The instant claims are directed to the synthesis of L-threofuranosyl nucleosides and 3'-phosphonate substituted nucleotides, intermediates necessary in the execution of said syntheses, pharmaceutical compositions thereof, and methods of treating viral infections, including HIV infections, by administration of an effective amount of one of said nucleotide analogues to a host in need thereof.

C. The state of the prior art: The prior art of record herein presently includes disclosures of both erythro- and threo-furanosyl nucleosides and nucleotides and analogues thereof, and also disclosures of some medicinal activity thereof.

D. The level of one of ordinary skill would be expected to include knowledge of the organic synthesis of nucleosides, nucleotides and analogues thereof, and the medicinal testing of said compounds *in vitro*.

E. The level of predictability in the art: The relatively small quality of prior art presently of record the is directly relevant to the instant claimed compounds and to the synthesis thereof supports the view that the instant art area is not well explored at present and therefore likely to be unpredictable, particularly in the area of medicinal activity.

F. The amount of direction provided by the inventor: The instant disclosure enables the synthesis of a very small number of L-threofuranosyl nucleoside and nucleotide derivatives, and also enabled the administration of two of these products to the treatment of HIV.

G. The existence of working examples: This subject is dealt with in previous paragraph.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is found to be excessive because the instant disclosure does not

provide a sufficient comprehensive disclosure to adequately enable such broadly and indefinitely drafted claims as noted in the analysis provided above.

The disclosure is objected to because of the following informalities:

At page 97 at line 12, the term "comound" appears to be a misspelling of the term -- compound --. Applicant is respectfully requested to carefully proof-read the instant disclosure for other similar typographical and/or grammatical errors.

Appropriate correction is required.

Claims **14-23** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim **14** at line 1, the term "including" is inappropriate open language in a compound claim because said term implies that the subsequent description is missing details; i.e. that the generic class being claimed is not entirely defined by the claim. Applicant is respectfully requested to avoid this problem in compound claims by substitution of the term -- having the structure -- or the like.

In claim **14** at line 1-9, most of the preamble is superfluous in view of the generic formulas at lines 11 and 13 and therefore may be deleted without compromising the scope of claimed subject matter.

In claim **14** at line 15, the term "oxygen" and "sulfur" refer to elements. Did applicant intend the terms to read -- -O- -- and
-- -S- --, respectively?

In claim **14** at line 19, the terms "heterocyclic" and "heterocyclic-alkyl" are incompletely defined because the identities, the ring size(s), the degree(s) and the location(s) of unsaturation(s), and the location(s) of the hetero atom(s) have not been specified in the claim.

In claim **14** at lines 21-23, the names ending in "carbonate" are directed to compounds, not substituent moieties. Appropriate amendments are respectfully requested.

In claim **14** at lines 17 and 29 a Markush preamble is provided, but at lines 23 and 30 there is no -- and -- between the last two Markush group members. Appropriate addition of the term -- and -- is respectfully requested. See also claim

In claim **14** at lines 24-26 and lines 31-33, the term "heteroatoms" is incorrectly and incompletely defined because the heteroatoms are not the elements, and because the "-O-" and "-S-" substituent moieties may or may not have a terminal substituent and in the case of "N" may have one additional substituent if within the chain and two terminal substituents when at the end of the chain, substituents not defined by the claim. Therefore the claim is incompletely defined.

In claim **14** at lines 43-44, the definition provided is unclear. Applicant is respectfully requested to amend to make the meaning unequivocal.

In claim **14** at lines 46-47, the Markush preamble is not accompanied by the term -- and -- at line 47. Deletion of the preamble or substitution of -- and -- for the term "or" is respectfully requested. See also claim **21** wherein a similar error occurs.

In claim **14** at line 55, the term "provided that" is a proviso. Examiner respectfully requests thtat the proviso be moved to a separate indented line to insure that anyone reading the claim will not miss it.

In claim **14** at line 61-62, the term "solvates, stereoisomers and prodrugs thereof" is directed to subject mater that has not been adequately defined within the claim and therefore said term renders the claim incomplete. See also claim **15** for the same error.

In claim **15** the term "A compound of claim **14**" is in improper form for a dependent US patent claim. Applicant is respectfully requested to amend the claim to read -- The compound of claim **14** --.

In claim **15** at line 32, the term "(XVII), and" is incorrect because there is no Markush preamble. Applicant is respectfully requested to either add the appropriate Markush preamble or to substitute the term -- or -- for the term "and" to insure proper format of what appears to be intended as an alternative listing. See also claim**16** wherein the same error occurs.

In claim **17** at lines 3, 4, 6, 8 and 9, the term "derivatives" implies the presence of more than one substituent moiety, but the instant claim fails to define either the particular entities of the moieties intended by the noted term or the total number thereof, thereby rendering the claim indefinite because of incompletely defined metes and bounds. See also claims **18 and 19** wherein the same error reoccurs.

In claim **20** at line 22, the term "Phos" is incompletely defined by the terms at the end of the noted line because the complete structures of the named functional groups cannot be entirely determined from the terms provided.

In claim **21** the term "l-threose" at the end of each chemical name renders each name incomplete. Did applicant intend to claim only cyclic sugar substituted nucleotide analogues and therefore to have the term read -- L-threofuranose --?

In claim **22** the term "in a mammal" is incomplete and needs to be amended to read -- in a mammal in need thereof --. In claim **23** the term to be added might read as follows: -- in a host in need thereof --, or the like.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

(e) the invention was described in

(1) an application for patent described under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application filed under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)."

(f) he did not himself invent the subject matter sought to be patented."

Claim **26** is rejected under 35 U.S.C. §102(**b**) as being anticipated by **Dujardin et al.** (PTO-1449 ref. **AR**).

Applicant is referred to the cited reference at page 1557 wherein compounds **8g, 8h, 9g and 9h** each anticipate the structure at line 3 of claim **26** (first structure provided).

Claims **14-25** would be allowable if rewritten or amended to overcome the rejections under 35 U.S.C. §112 and §101 set forth in this Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. §1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §§102(f) or (g) prior art under 35 U.S.C. §103(a).

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published

applications may be obtained from either Private PAIR or Public PAIR. Status Information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see < http://pair-direct.uspto.gov >. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

LECrane:lec
06/20/2009

/Lawrence E. Crane/

Primary Examiner, Art Unit 1623

L. E. Crane
Primary Patent Examiner
Technology Center 1600